

CLAIMS

What is claimed is:

1. A method to protect a host cell, tissue or organism from an inflammatory condition comprising using a polynucleotide comprising at least one gene of an E3 region of an adenovirus, taken individually or in combination to protect a host cell, tissue or organism from an inflammatory condition.
2. The method of claim 1, wherein said at least one gene is a gene encoding a functional 14.7K, 14.5K, or 10.4K protein.
3. The method of claim 2, wherein said at least one gene encodes a functional 14.7K protein.
4. The method of claim 2, wherein said at least one gene is a gene encoding a functional 14.5K protein and gene encoding a functional 10.4K protein.
5. The method of claim 4, wherein said functional 14.5K protein and said functional 10.4K protein associate in a host cell to form a receptor internalization and degradation complex (RID complex).
6. The method of claim 1, wherein said at least one gene is operably linked to the immediate early promoter of the cytomegalovirus (CMV promoter).
7. The method of claim 1, wherein said polynucleotide is inserted into an expression vector.

8. The method of claim 7, wherein said polynucleotide is inserted into an expression vector which further comprises a gene of interest operably linked to regulatory elements for expression in a host cell.

5 9. The method of claim 7, wherein said expression vector is a plasmid or a viral vector.

10. The method of claim 9, wherein said viral vector is an adenoviral vector.

11. The method of claim 10, in which all or part of an E1 region and all of the native E3 region in the adenoviral vector are deleted or non-functional.

10 12. The method of claim 11, wherein at least one viral gene of the E2, E4, and L1-L5 regions in the adenoviral vector is deleted or non-functional.

13. The method of claim 10, wherein said adenoviral vector is a modified adenovirus genome of the human adenovirus 5 (Ad5) and said at least one gene of the E3 region is isolated from the genome of the human adenovirus 2
15 (Ad2).

14. The method of claim 10, wherein said polynucleotide encodes a functional 14.7K protein and is inserted into said adenoviral vector either (i) at a location where the E3 region normally resides and in anti-sense orientation relative to the transcriptional direction of the native E3 region or (ii) where the E1 region
20 normally resides and in sense orientation relative to the transcriptional direction of the native E1 region.

15. The method of claim 10, wherein said polynucleotide encodes a functional 14.5K protein and a functional 10.4K protein and is inserted into said adenoviral vector at a location where the E3 region normally resides and in sense orientation relative to the transcriptional direction of the native E3 region.

5 16. The method of claim 1, wherein said inflammatory condition is mediated by Tumor Necrosis Factor (TNF).

17. The method of claim 16, wherein said TNF is TNF- α .

18. The method of claim 1, wherein said inflammatory condition is mediated by Fas.

10 19. The method of claim 1, wherein said inflammatory condition is mediated by a gene therapy vector.

20. The method of claim 1, wherein said inflammatory condition is septic shock, fulminant hepatic failure, hepatitis, cirrhosis, an alcoholic liver disease, chemotherapy-induced toxicity, graft rejection, an immune disorder, a
15 neoplastic disease, or a connective tissue disorder.

21. A method for gene transfer comprising using the recombinant adenoviral vector to transfer at least one gene to a cell wherein at least a part of the E3 region of the adenoviral vector is deleted or is rendered non-functional, and wherein said adenoviral vector retains E3 sequences encoding:

- 20 (i) a functional 14.7K protein, and optionally
 (ii) a functional 14.5K protein and a functional 10.4K protein,

wherein said recombinant adenoviral vector comprises a gene of interest; wherein said retained E3 sequences and said gene of interest are operably linked to regulatory elements allowing their expression in a host cell; wherein said retained E3 sequences encoding a functional 14.7K protein are located in said adenoviral vector either (i) at a location where the E3 region normally resides and in antisense orientation relative to the direction of transcription of the native E3 region or (ii) wherein the E1 region normally resides and in sense orientation relative to the direction of transcription of the native E1 region; and wherein said retained E3 sequences encoding a functional 14.5K protein and a functional 10.4K protein are located in said adenoviral vector at a location where the E3 region normally resides and in sense orientation relative to the direction of transcription of the native E3 region.

22. A recombinant adenoviral vector in which at least a part of the E3 region is deleted or is rendered non-functional, wherein said adenoviral vector retains E3 sequences encoding:

a functional 14.5K protein and a functional 10.4K protein,
wherein said recombinant adenoviral vector comprises a gene of interest; wherein said retained E3 sequences and said gene of interest are operably linked to regulatory elements allowing their expression in a host cell; and wherein said retained E3 sequences encoding a functional 14.5K protein and a functional 10.4K protein are located in said adenoviral vector at a location where the E3 region normally resides and in sense orientation relative to the direction of transcription of the native E3 region.

23. The recombinant adenoviral vector of claim 22, wherein all of the E3 region is deleted or is rendered non-functional, with the exception of the E3 sequences encoding functional 14.5K and 10.4K proteins.

24. The recombinant adenoviral vector of claim 23, wherein the
5 functional 14.5K and 10.4K proteins associate in a host cell to form a receptor internalization and degradation complex (RID complex).

25. The recombinant adenoviral vector of claim 22, wherein the retained E3 sequences are placed under the control of the immediate early promoter of the cytomegalovirus (CMV promoter).

10 26. A method for preparing a viral particle, comprising:
(i) introducing the adenoviral vector of claim 22, into a permissive cell, to obtain a transfected permissive cell;
(ii) culturing said transfected permissive cell for an appropriate period of time and under suitable conditions to allow the production of said
15 viral particle;
(iii) recovering said viral particle from the cell culture; and
(iv) optionally, purifying said recovered viral particle.

27. A viral particle comprising the adenoviral vector of claim 22.

28. An isolated host cell comprising the adenoviral vector of claim 22.

20 29. A composition comprising the adenoviral vector of claim 22 and a carrier therefor.

30. The recombinant adenoviral vector of claim 22, in which all or part of the E1 region is deleted or is rendered non-functional.

31. The recombinant adenoviral vector of claim 30, wherein at least one gene of the E2, E4, and L1-L5 regions is deleted or rendered non-functional.

5 32. The recombinant adenoviral vector of claim 22, in which all or part of the E1 region and all of the native E3 region are deleted or rendered non-functional, wherein the recombinant adenoviral vector is a modified adenovirus genome of human adenovirus 5 (Ad5) and said retained E3 sequences are isolated from the genome of the human adenovirus 2 (Ad2).

10 33. The recombinant adenoviral vector of claim 32, wherein at least one gene of the E2, E4, and L1-L5 regions is deleted or rendered non-functional.

34. A method for gene transfer comprising using the recombinant adenoviral vector of claim 22 to transfer at least one gene to a cell.